EURORDIS
RARE DISEASES EUROPE

Monthly update

Research & development of vaccines to prevent SARS-coV2 infection

Updated January 2021

Disclaimer

No vaccine against COVID-19 is approved. This document does not provide guidance on what vaccine or medicines to take. Please avoid self-prescription and always refer to your doctor before making any treatment decision.

This document provides a selection of updates on the research and development of vaccines for the current coronavirus infection. Those highlights are for the information of patient organisations/ groups, advocates and people living with a rare disease. EURORDIS takes reasonable steps to verify the accuracy of the information presented. This document does not constitute, and shall not be deemed or construed as, any approval or endorsement by EURORDIS of such product or entity.

Contents (click to navigate in document)

A 'must-read' introduction

This document provides a selection of updates on the research and development of vaccines to prevent SARS-coV2 infection that causes COVID-19. Those highlights are for the information of patient organisations/ groups, advocates and people living with a rare disease. EURORDIS takes reasonable steps to verify the accuracy of the information presented. This document does not constitute, and shall not be deemed or construed as, any approval or endorsement by EURORDIS of such product or entity.

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EURORDIS has a role in disseminating up-to-date information that could be useful for people living with a rare disease, who are exposed to the SARS-coV2 virus infection. Some rare diseases constitute an aggravated risk when infected by C-19. Some products being studied for C-19 are already approved or used off-label for some rare diseases, with potential information confusion and shortages risks. In other rare diseases, some products being studied for C-19 may have medicinal products interactions with medicines used in the care of these diseases. All good reasons to inform patient advocates with curated though raw information material to empower their respective actions. EURORDIS's Task Force on Drug Information, Transparency and Access (DITA) was tasked to prepare and regularly update this document. This task force is composed of EURORDIS volunteers and staff.

This document is an editorial selection and highlights the most recent developments for products being currently tested in phase III clinical trials, measuring their efficacy and toxicity. It is by no mean an exhaustive list of all therapeutic research. To avoid repeating the same situation than for the last Ebola outbreak, where the evaluation of potential treatments could not be completed (not enough participants as the trials were started too late), clinical trials against COVID-19 were authorised very soon after the epidemic started. The priority is to enrol participants in authorised trials.

For any questions or clarification, please contact François Houÿez: francois.houyez@eurordis.org

Resources

- EUnetHTA Covid-19 Rolling Collaborative Reviews https://eunethta.eu/rcr01-rcrxx/
- Horizon scanning for treatments and vaccines by the Austrian HTA institute GÖG https://eprints.aihta.at/1234/
- World Health Organization: https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf?ua=1
  All trials for COVID-19: https://www.who.int/docs/default-source/coronaviruse/covid-19-trials.xls?sfvrsn=a8be2a0a_6&ua=1
- The NIH register of clinical trials includes 210 clinicals trials to treat COVID 19 (as of 30 March 2020). You can consult here: https://clinicaltrials.gov

And also

- A review of the most advanced research was published here in March 2020:

  Research and Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases. Cynthia Liu et al. ACS Cent. Sci., 315-331. Published 12/03/2020
  https://pubs.acs.org/doi/10.1021/acscentsci.0c00272

- Other information (infography): https://www.visualcapitalist.com/every-vaccine-treatment-covid-19-so-far
- Video on the pathophysiology of the virus, the dynamic of the pandemic and how to fight it

  https://youtu.be/BtN-goy9VOY

Vaccines in development

This document is a summary of information on vaccines in development to prevent the SARs-coV2 infection, intended for people living with a rare disease. Sources include the European Medicines Agency and EUnetHTA, the European Network of HTA Agencies that publishes rolling collaborative reviews and horizon scanning reports.

Of all vaccines in development to prevent the infection, the EURORDIS's Drug Information, Transparency and Access Task Force decided the following selection for its own review:

1. The most advanced vaccine candidates: products in clinical development already, with emphasis on products in phase II, phase II/III and/or phase III.
2. Products with specific issues on efficacy or safety for some groups of rare diseases

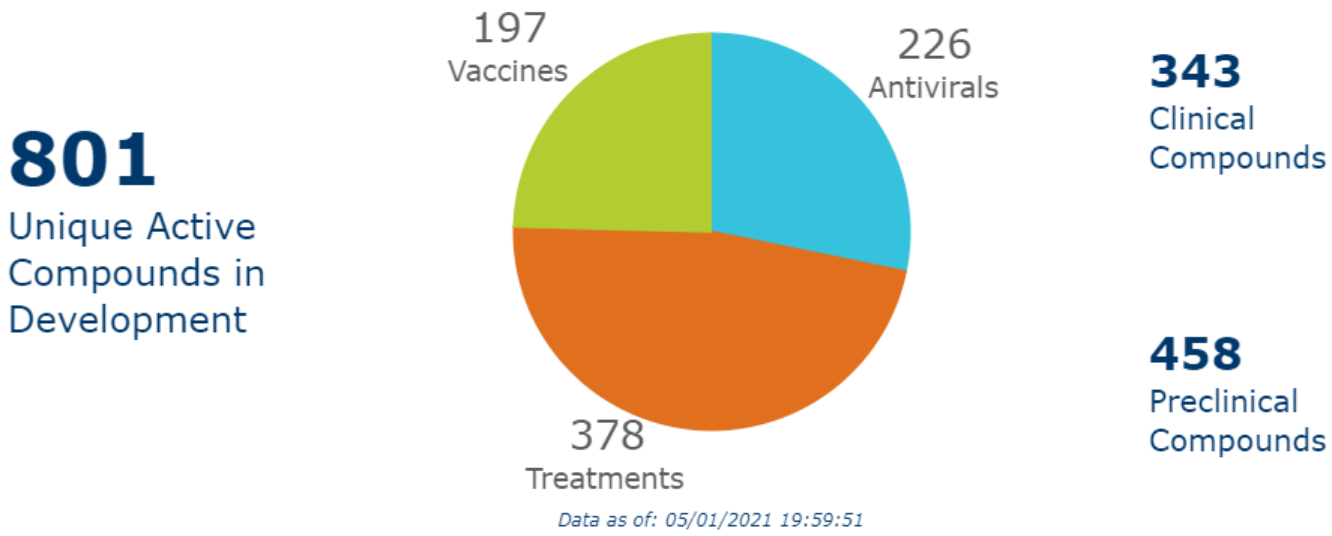


Figure 1: https://www.bio.org

Latest news

January 12th: EMA receives application for marketing authorisation of AstraZeneca's vaccine

https://www.ema.europa.eu/en/news/ema-receives-application-conditional-marketing-authorisation-covid-19-vaccine-astrazeneca

January 8th: Second EMA public debate on vaccines for COVID-19

https://www.ema.europa.eu/en/news/ema-organises-second-public-meeting-about-new-covid-19-vaccines

January 6th: Moderna vaccine authorised in the EU

https://www.ema.europa.eu/en/news/ema-recommends-covid-19-vaccine-moderna-authorisation-eu

December 30th: AstraZenaca / Uni Oxford authorised in the United Kingdom (emergency supply)

https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca

December 24th: Comirnaty®, Pfizer/BioNtech vaccine authorised in the EU

https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty

December 1st: EMA starts rolling review of the J&J vaccine

https://www.ema.europa.eu/en/news/ema-starts-rolling-review-janssens-covid-19-vaccine-ad26cov2s

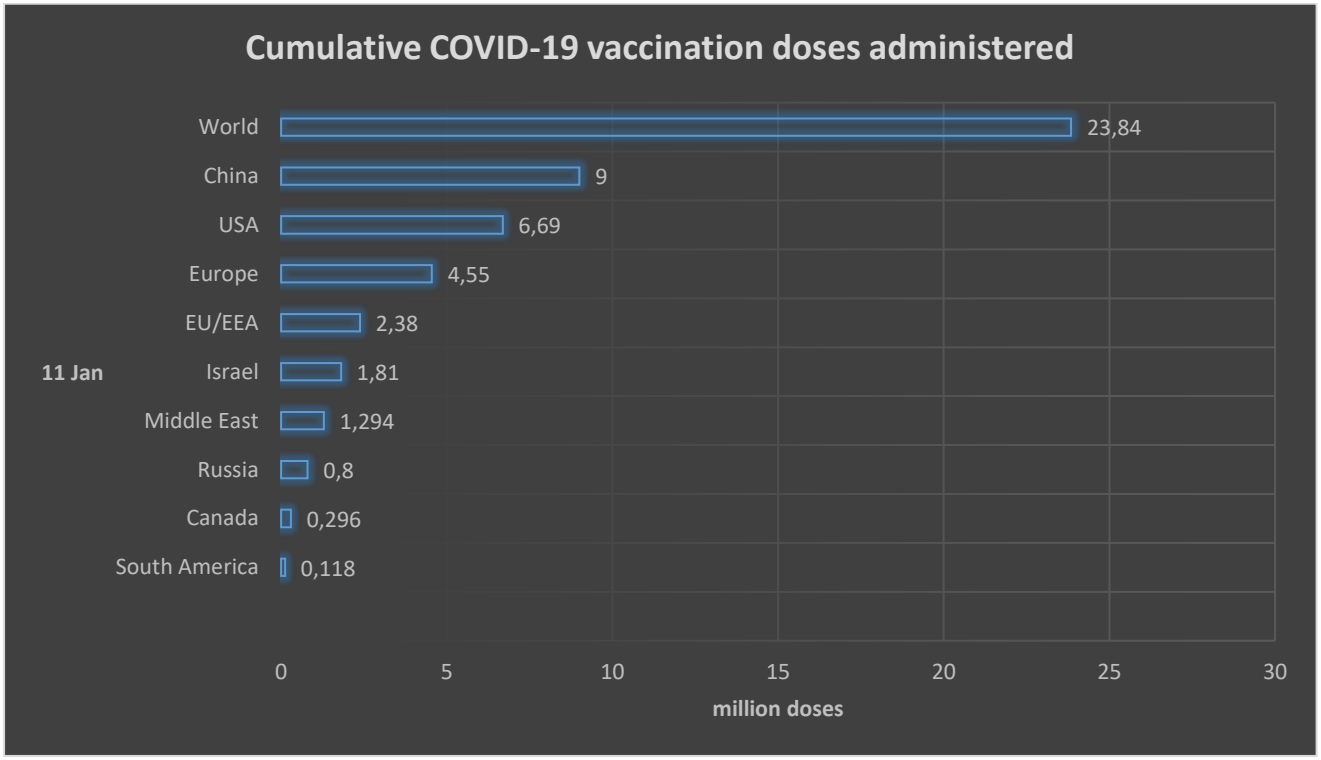
Vaccine platforms

Platform		Description	Examples
Inactivated		Whole virus, killed (heated or chemically). It cannot cause illness. In general, inactivated viruses do not provide as strong immune response as an attenuated virus vaccine, so repetition of doses needed	Polio virus influenza
Live attenuated		Live attenuated vaccines are made up of whole viruses that have been weakened in a lab (usually through culturing). In general, stronger immune response than inactivated vaccines	Tuberculosis Varicella MMR (Measles, mumps, rubella) Influenza
Subunit		Fragment or portion of the virus introduced into the body. This fragment is enough to be recognised by the immune response and stimulate immunity	Pertussis HPV Hep. B
Viral vector		Viral vector vaccines insert a gene for a viral protein into another, harmless virus (replicating or non-replicating). This harmless virus then delivers the viral protein to the vaccine recipient, which triggers an immune response.	Ebola Veterinary vaccines Recombinant influenza vaccine
mRNA		Work by introducing an mRNA sequence (the molecule that tells cells what to build) coded for a disease specific antigen. Once this antigen is reproduced within the body, it is recognised and triggers an immune response.	None
DNA		Work by inserting synthetic DNA of viral gene(s) into small DNA molecules called plasmids. Cells take in the DNA plasmids and follow their instructions to build viral proteins, which are recognised by the immune system, and prepare it to respond to disease exposure.	None

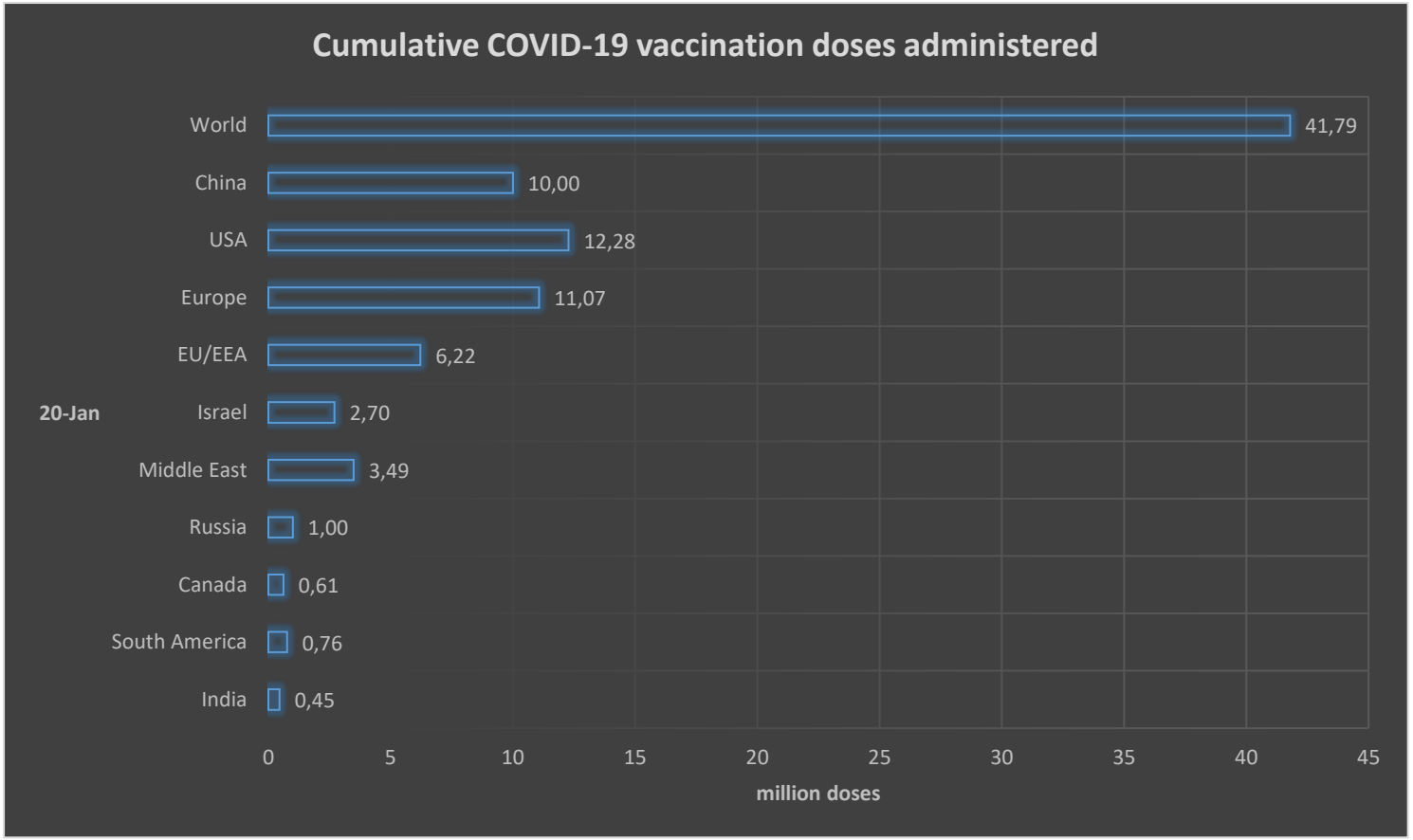
Vaccination campaign

Cumulated number of doses administered, world regions

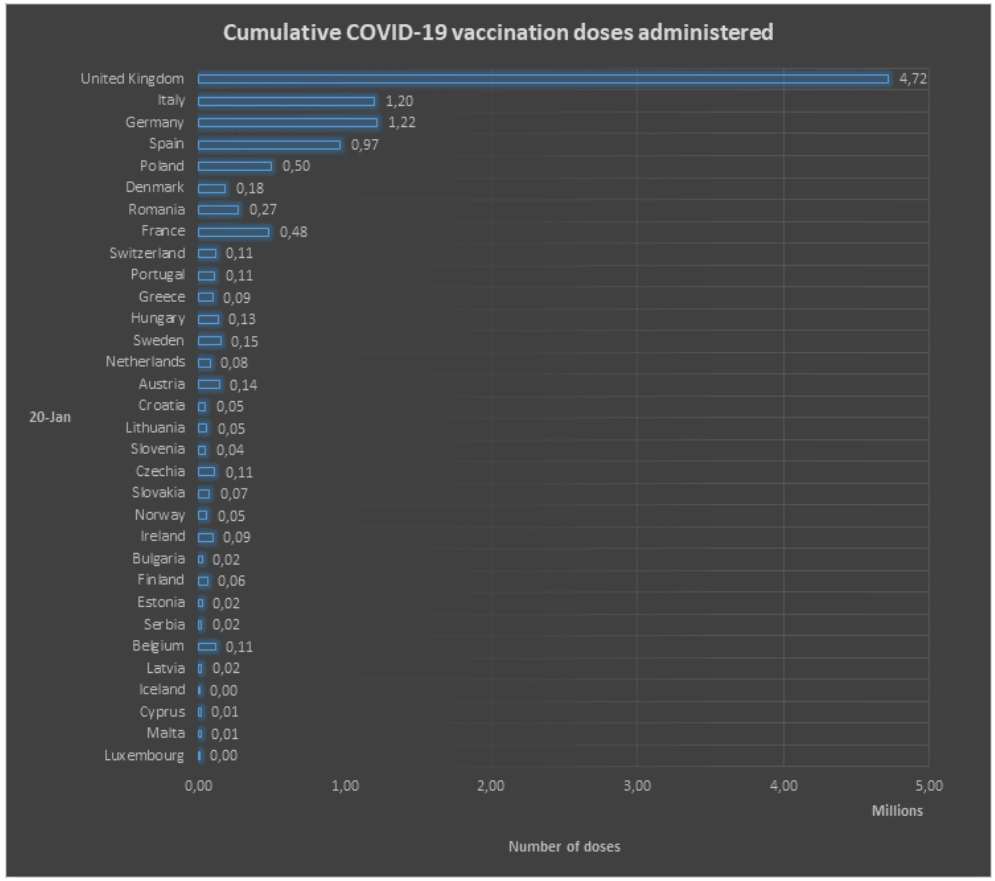
As of 11 January

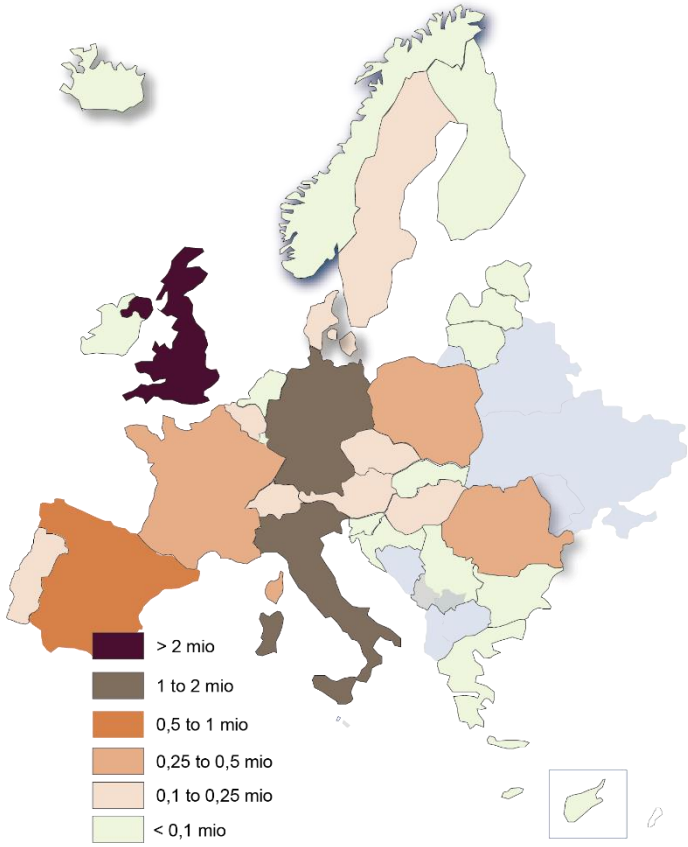


As of 20 January

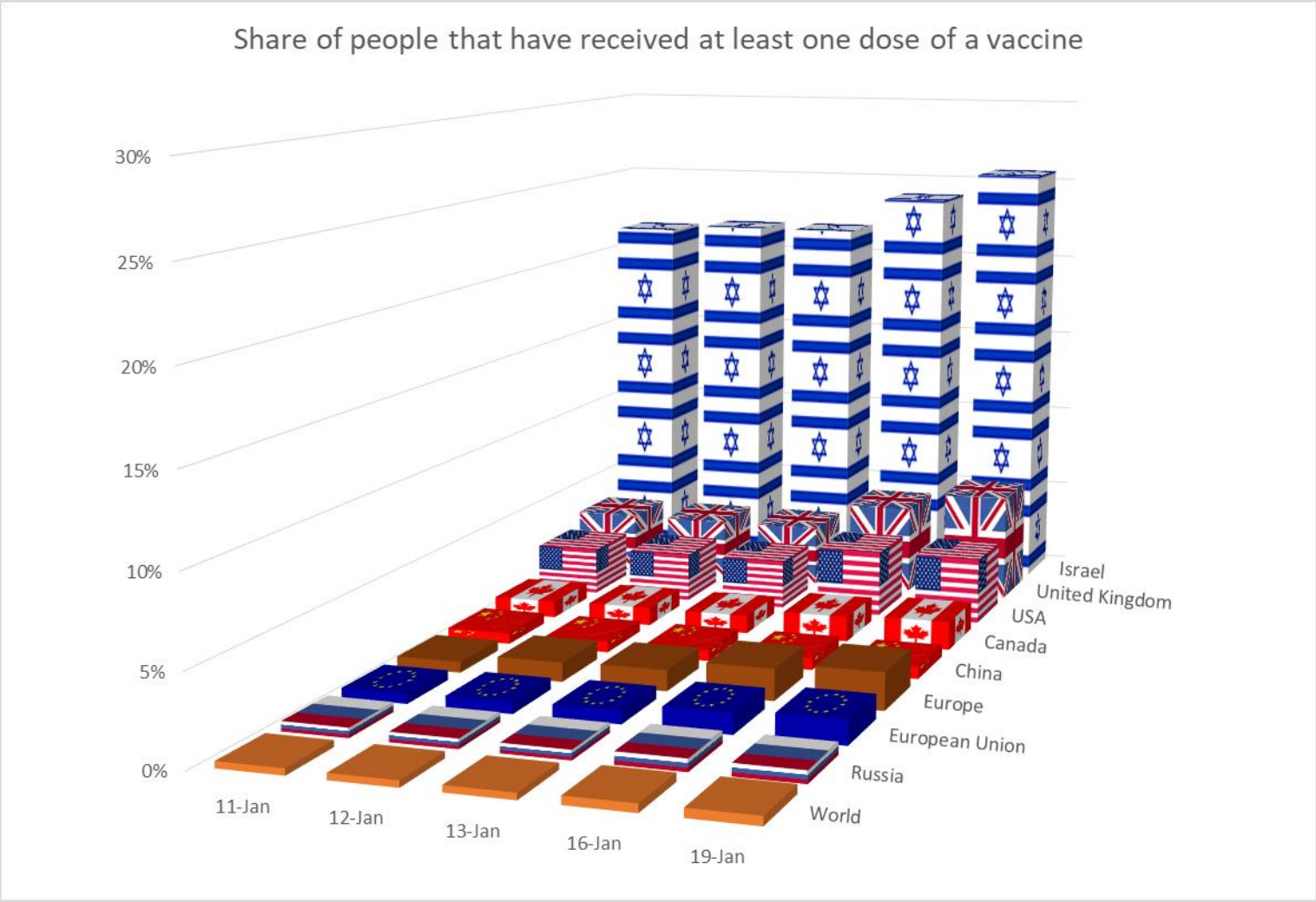


Cumulated number of doses administered, Europe, by country

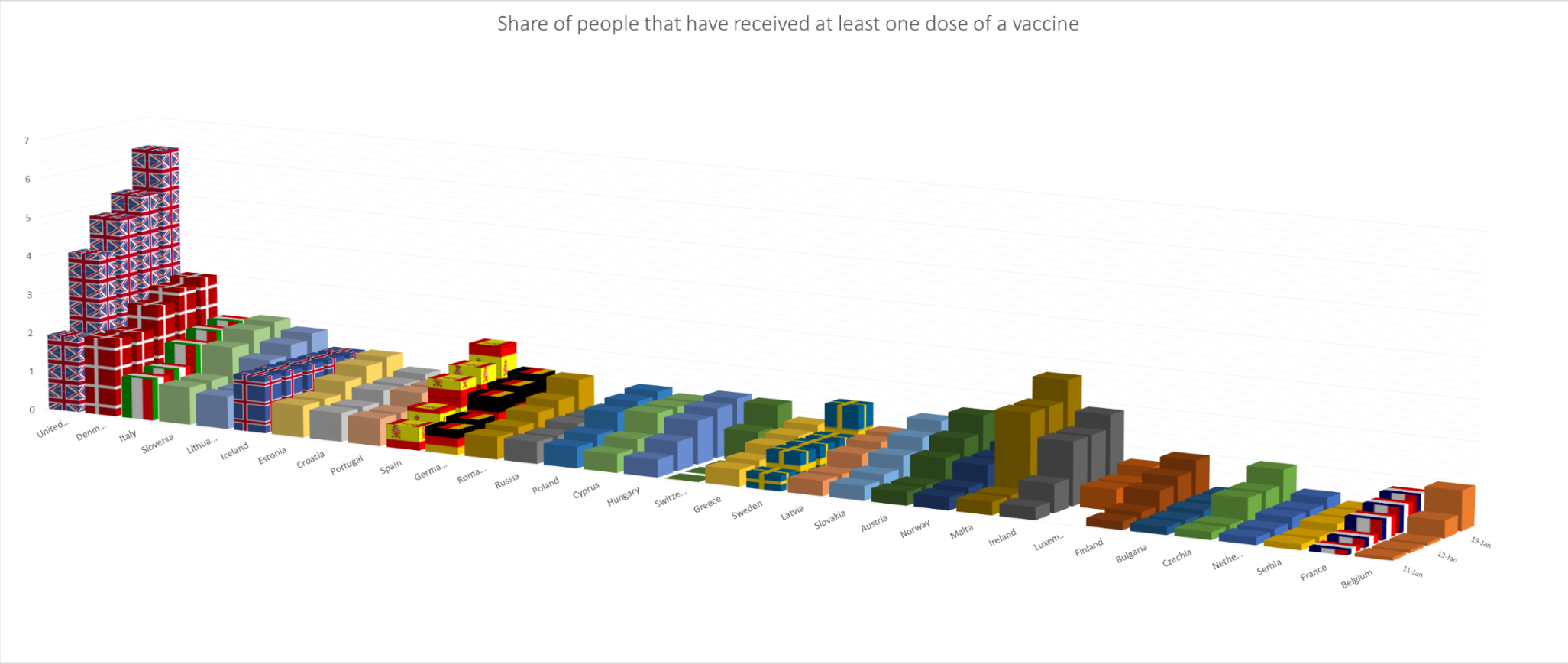


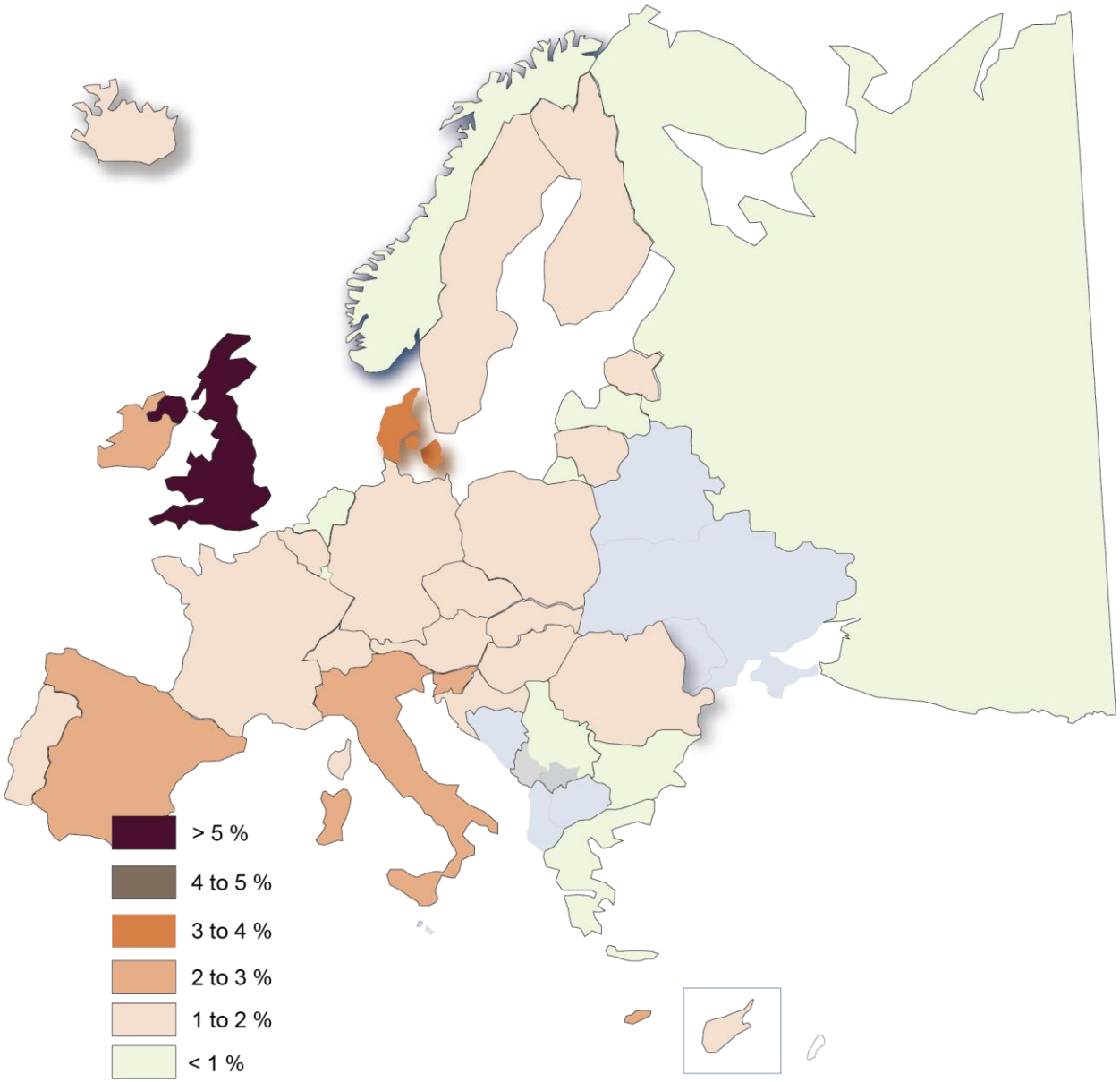


Share of the population that received at least one dose, world regions



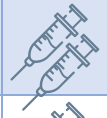
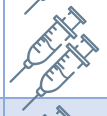
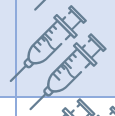
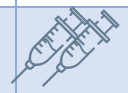
Share of the population that received at least one dose, Europe




> 5 %
4 to 5 %
3 to 4 %
2 to 3 %
1 to 2 %
< 1 %

Vaccines

Information on authorised vaccines, vaccines undergoing evaluation or rolling review

Company	Brand name	Number of doses	Research status	Investments	Emergency use authorisation or full authorised in	Information
In use in human						
BioNtech/Pfizer Warp Speed Finalist	Comirnaty®		Ph. II/III ongoing: 44,000 volunteers in USA, Argentina, Brazil, Germany, South Africa, Turkey	Pfizer: $500M US Gov.: $1.9B	EU, USA, Bahrain, Canada, Chile, Costa Rica, India, Japan, Mexico, Philippines, Qatar, Saudi Arabia, Singapore, Switzerland, UK. WHO Emergency Validation	See product information (EMA): here
Moderna Warp Speed Finalist COVAX Portfolio	-		Ph. III ongoing: 30,000 USA only	US Gov.: $2.48B CEPI: undisclosed	Canada, USA, United Kingdom, European Union	See product information (EMA): here
AztraZeneca Warp Speed Finalist COVAX Portfolio	-		Ph. III ongoing: 40,000 in United Kingdom south Africa, and 10,000 in Brazil	US Gov.: $1.2B CEPI/GAVI: $750M EU: $923M	Argentina, India, United Kingdom	See UK product information: here Conditional MA application in EU
Sinopharm / Beijing Institute of Biologic Products			Ph III ongoing: 45,000 in UAE, Bahrain, Jordan, Egypt, Argentina, Peru	-	Egypt, Bahrain, China, UAE	
Gamaleya Research Institute	Sputnik V		Ph III ongoing in Russia, Belarus, UAE, Venezuela	-	Argentina, Belarus, Russia	
Sinovac Biotech	CoronaVac		Ph III ongoing in 28,000 in Brazil, Indonesia, Bangladesh, Turkey, China	-	China	
Rolling review in progress						
Janssen-Cilag			Ph III ongoing: 60,000 in USA, Argentina, Brazil, Chile,	J&J: $500M US Gov.: $1.45B	Rolling review started at EMA on 1/12/2020	Product does not need to be stored at sub-zero temperatures,

Warp Speed Finalist			Colombia, Mexico, Peru, South Africa			and it may require just a single dose.

WHO is tracking 34 candidates in various stages of development. Here are information on the most advanced candidates (phase I-2, phase 2-3 or phase 3) with their estimated completion date (interim analysis will be performed before the end-date).

Company	Vaccine	Platform	Phase	Completion date*	Country	Reference
Moderna	mRNA-1273	RNA	Phase 3	October 2022	USA	NCT04470427
CansinoBio	Ad5-nCov	Non-replicating viral vector	Phase 2		China	
Inovio	Ino-4800	Synthesised DNA plasmid vaccine	Phase 1		China, South Korea	
Janssen-Cilag J&J	JNJ-78436735	Ad26 vector expressing SARS-CoV-2 spike protein	Phase 3		USA,	NCT04505722
Novavax		VLP recombinant nano-protein	Phase 1-2		Australia, USA	NCT04368988
GSK/Dynavax		molecular clamp	Phase 1		Australia	
CureVac	CVnCoV	mRNA-based vaccine	Phase 1		Belgium, Germany	
BioNtech/Pfizer	BNT-162	mRNA based vaccine	Phase 2-3	November 2022	USA, Germany	NCT04368728
Sinovac Biotech	CoronaVac	Inactivated virus	Phase 3	October 2021	China, Brazil	NCT04456595
GSK / Sanofi		Recombinant protein, adjuvant	Phase 1-2	Ph III delayed, lack of immunogenicity in higher age groups	USA	
AztraZeneca	ChadOx1nCov-19	Non-replicating viral vector	Phase 3	August 2021	GBR	NCT04400838
Shenzen Inst.	LV-SMENP-Dc	Lentivirus	Phase 1-2		China	
Research	BCG vaccine	Live attenuated	Phase 2-3	April 2021	Netherlands	NCT04328441
Murdoch CRI	BCG vaccine	Live attenuated	Phase 2-3	June 2021 or March 2022	Australia	NCT04327206
Sinopharm	Vero-Cell	Inactivated virus	Phase 3	July 2021	China	ChiCTR2000034780
Gamaleya	Gam-COVID-Vac (Sputnik V)	Ad26 vector expressing SARS-CoV-2 spike protein	Phase 3		Russia	

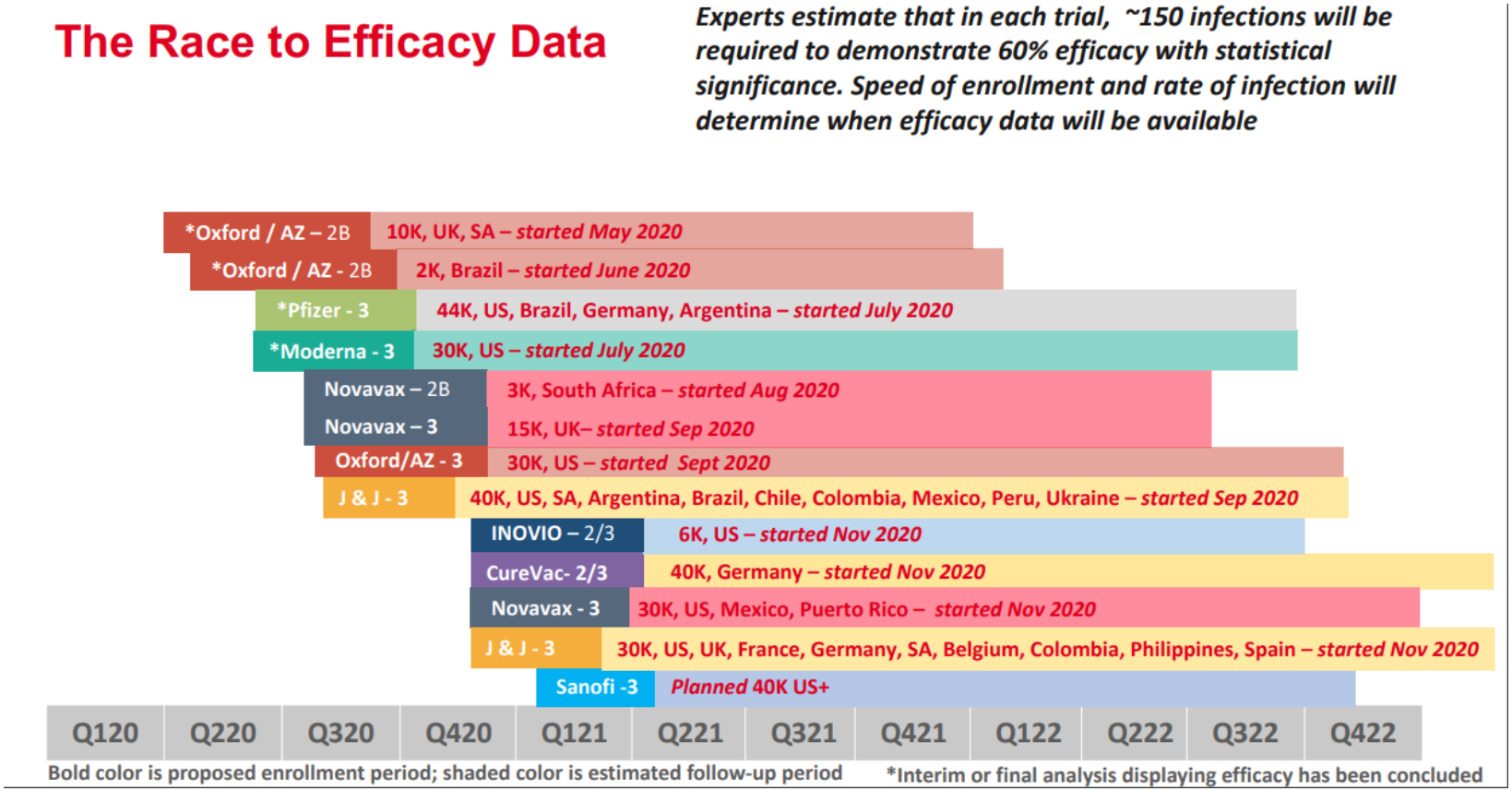


Figure 2: courtesy AVAC. In this graph, Sanofi's phase III trial is still indicated to start during the first quarter 2021, however Sanofi announced it would be delayed to end-2021.

Pfizer/BioNTech

Authorised in EU

Brand name

Comirnaty®

Developer

Developed by BioNTech in collaboration with Fosun Pharma and Pfizer

Description

mRNA platform-based vaccine expressing codon-optimized undisclosed SARS-CoV-2 protein(s)

Development phase

BNT-162 entered clinical testing by the end of April 2020.

A phase 2/3 RCT has started (NCT04368728/EudraCT 2020-002641-42) with aim to describe the safety, tolerability, immunogenicity and efficacy of BNT-162. It enrolled 44,000 participants above 12 years of age in USA, Argentina, Brazil, Germany, South Africa, and Turkey and its primary efficacy endpoint was reached.

Regulatory status

This vaccine can be used in human in the following jurisdictions: EU, USA, Bahrain, Canada, Chile, Costa Rica, India, Japan, Mexico, Philippines, Qatar, Saudi Arabia, Singapore, Switzerland, United Kingdom.

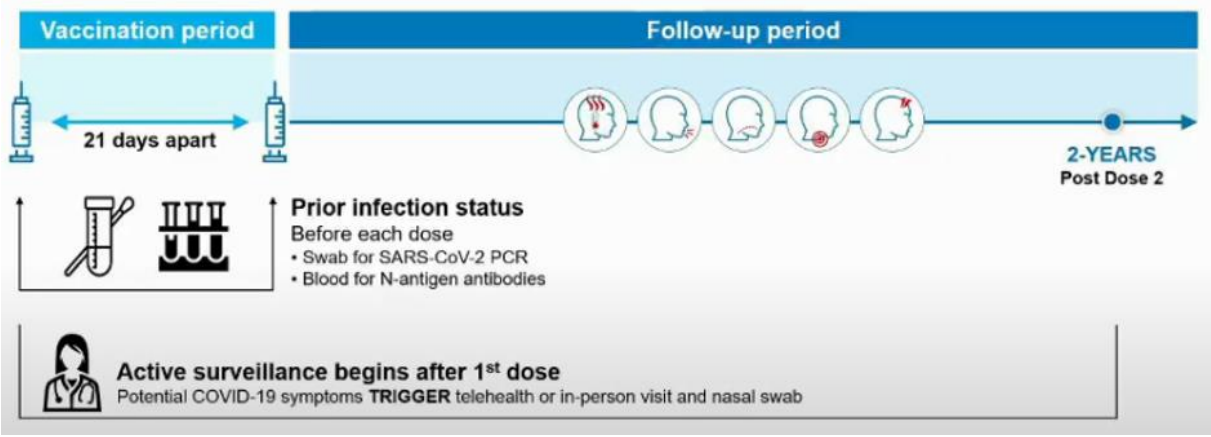
December 24th: Comirnaty®, Pfizer/BioNtech vaccine authorised in the EU. See EMA information here: https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty

Efficacy and safety data

Equally effective for all age groups, effect lasts for at least 3 months after 2nd dose (as of December 2020).

Two doses are needed, all participants were checked for coronavirus infection before each dose via PCR and antibodies detection. Symptoms of COVID-19 were investigated via tele-medicine, in-person visits and nasal swabs.

Participants will be followed-up for up to 2 years after the second dose.



Primary efficacy analysis patrticipants with 2 doses	mRNA	placebo	Comments - interpretation
Number of participants	18,198	18,325	
Confirmed symptomatic COVID-19 cases	8 (0.044%)	162 (0.88%)	
Reduction of the risk	**95%**		For 20 people who had the COVID-19 disease in the placebo group, there was only 1 in the group that received the vaccine
Among adults from 18 to 65 yo			
Confirmed symptomatic COVID-19 cases	7	143	
Reduction of the risk	95.1%		
Among adults above 65 yo			
Confirmed symptomatic COVID-19 cases	1	19	
Reduction of the risk	92.9%		
Among males	3	81	Reduction: 96.4%
Among females	5	81	Reduction: 93.7%

Pfizer/NioNtech vaccine protects against severe forms of COVID-19:

Primary efficacy analysis in participants with at least one dose	mRNA	placebo	Comments - interpretation
Number of participants	21,314	21,259	
Confirmed severe COVID-19 cases	1 (0.0047%)	9 (0.0423%)	
Reduction of the risk		**88.9%**	For 10 people who had a severe COVID-19 disease in the placebo group, there was only 1 in the group that received the vaccine

Side-effects more frequent in the mRNA arm than in the placebo arm included pain (at injection site), fatigue, headache, chills, muscle and joint pain. Globally, more people in the vaccine group had general disorders (18.3% versus 3.9% in the placebo group), or musculo-skeletal and connective tissue disorders (7.3% versus 2%), or nervous system disorders (6.1% versus 2.4%).

More research continues among children, in pregnancy, in immune-compromised patients and on a new formulation that is more stable in the refrigerator.

How it is used

Doses taken 21 days apart. Local storage conditions:

- Freezer at -70°C up to expiration date

Moderna

Authorised in EU

Description

The ModernaTX, Inc.mRNA-1273 vaccine candidate developed by ModernaTX, Inc. in collaboration with NIAID is an encapsulated mRNA-based vaccine (mRNA-1273). It is intended for the prevention of infection through a protein of SARS-CoV-2 that is the key into the human cell. An mRNA-based virus has not been approved for use in humans yet. It is a synthetic RNA strand designed to elicit an immune-response to produce antibodies against SARS-coV2.

To learn more on mRNA vaccines and how they were discovered, an informative video by the NIH Vaccine Research Centre here: https://www.youtube.com/watch?v=uXcA-mByGfw&feature=youtu.be

Development phase

Currently, there is a phase III trial with 30,000 participants (NCT04470427):

- Design: randomised to 1:1 placebo-controlled trial
- Enrolment: approximately 30,000 participants enrolled in the U.S
- To be continued for at least 18 months

Regulatory status

This vaccine can be used in human in the following jurisdictions: Canada, USA, United Kingdom, and the European Union (January 6th: Moderna vaccine was authorised in the EU. See here https://www.ema.europa.eu/en/news/ema-recommends-covid-19-vaccine-moderna-authorisation-eu)

Efficacy and safety data

Equally effective for all age groups, effect lasts for at least 3 months after 2nd dose (as of December 2020).

Primary efficacy analysis	mRNA	placebo	Comments - interpretation
Number of participants	14,134	14,073	
Confirmed symptomatic COVID-19 cases	11 (0.077%)	185 (1.3%)	
Reduction of the risk	**94.1%**		For 20 people who had the COVID-19 disease in the placebo group, there was only 1 in the group that received the vaccine

Among adults from 18 to 65 yo with no underlying disease	8,396	8,403	
Confirmed symptomatic COVID-19 cases	5	121	
Reduction of the risk	**95.9%**		Same
Among adults from 18 to 65 yo with underlying diseases	2,155	2,118	
Confirmed symptomatic COVID-19 cases	2	35	
Reduction of the risk	**94.4%**		Same
Among adults older than 65, with or without underlying disease	3,583	3,552	
Confirmed symptomatic COVID-19 cases	4	29	
Reduction of the risk	**86.4%**		For 7 people who had the COVID-19 disease in the placebo group, there was only 1 in the group that received the vaccine

Side-effects more frequent in the mRNA arm than in the placebo arm included pain (at injection site), most often mild, swelling, erythema (red skin), some fatigue, headache, muscle pain, joint pain and some fever.

A few death occurred in both arms, not related to the vaccine: 6 in the vaccine group (1 suicide, 1 cardio-vascular arrest, 1 head injury, 1 myocardial infarction, 1 multisystem organ failure, 1 not specified), and 7 in the placebo group (1 abdominal injury, 1 cardio-vascular arrest, 1 due to COVID-19, 2 myocardial infarctions, 1 dermatitis bullous, 1 not specified).

No participant was excluded from the trial due to allergic reactions prior to entering the trial. 2 anaphylactic reactions occurred (a serious and profound state of shock brought about by hypersensitivity to an allergen such as a drug, foreign protein, or toxin):

- One in the placebo group (10 days after first dose)
- One in the vaccine group (67 days after first dose)

The relation between the reaction and the vaccine is therefore not established.

How it is used

Doses taken 28 days apart. Local storage conditions:

- Freezer at -20°C up to expiration date
- Refrigerator 5°C up to 30 days
- Room temperature up to 12 hours
- Local transport at 5°C.

AztraZeneca vaccine

January 12th: EMA receives application for marketing authorisation of AstraZeneca's vaccine

https://www.ema.europa.eu/en/news/ema-receives-application-conditional-marketing-authorisation-covid-19-vaccine-astrazeneca

Developer

The ChAdOx1 nCoV-19 (AZD1222) is developed by AstraZeneca, licensed from Oxford University) vaccine candidate developed by the Jenner Institute at Oxford University.

Description

It is based on a non-replicating viral vector. A chimpanzee adenovirus platform is hereby used. This platform was previously utilised in clinical phase I trials for a vaccine against MERS.

The vaccine candidate uses a genetically modified safe adenovirus that may cause a cold-like illness. The intended prevention is through the modified adenovirus producing Spike proteins, eventually leading to the formation of antibodies to the coronavirus's Spike proteins.

Development phase

A Phase 2b/3 study (EUdraCT 2020-001228-32/NCT04400838) is ongoing, to determine the efficacy, safety and immunogenicity of ChAdOx1 nCoV-19. The primary endpoint is virologically confirmed (PCR positive) symptomatic COVID-19 infection.

A Phase 3 RCT (ISRCTN89951424) started in Brazil and South Africa, with another country in Africa set to follow, as well as a trial in the US. Participants are randomly allocated to receive the investigational vaccine or a well-established meningitis vaccine The study is estimated to be completed in July 2021.

Completion: August 20201. Interim analysis before, but completion needed for statistical power to analyse all 11 subgroups.

On 8 September 2020, the British-Swedish pharmaceutical company confirmed that one of the volunteers in a UK trial of the vaccine had developed an unexplained illness due to possible adverse reaction in one participant.[1]

All trials of this vaccine, which have so far included at least 17,000 people across the UK, Brazil and South Africa, have been halted.

This is the second time: there was a brief trial pause in July while a safety review took place after one volunteer was confirmed to have an undiagnosed case of multiple sclerosis, which the independent panel concluded was unrelated to the vaccine.

On September 12th, the U.K. Medicines Health Regulatory Authority recommended that the study resume after an independent review of the safety data triggered a pause on Sept. 6, Oxford said in a statement. It declined to disclose details about the volunteer's illness.

No announcement was made on the status of trials outside the U.K. Trials were underway in the U.S., Brazil, South Africa and India before being paused after the safety review.

Oxford said some 18,000 people have received "study vaccines" as part of the trials. The trial started just as rates of infection in the U.K. began dropping in May, making it harder to demonstrate whether the vaccine works.

Exclusion criteria

Many rare conditions are not compatible with the inclusion in this trial (it is a phase 2b/3, with intense toxicity monitoring).

Results

As of 17 August, 2020, a preliminary report with the results from the phase 1/2 single-blind, RCT (ISRCTN 15281137/NCT04324606/EudraCT 2020-001072-15) was published. 1,077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group.

There were no serious adverse events.

In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14. Anti-spike IgG responses rose by day 28 and were boosted following a second dose.

[1] ABC News Australia https://www.abc.net.au/news/2020-09-10/astrazeneca-oxford-covid-19-vaccine-trial-no-final-diagnosis/12648248

Authors concluded that ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses and together with the induction of both humoral and cellular immune responses, support largescale evaluation of this candidate vaccine in an ongoing phase 3 programme.[2]

Janssen-Cilag or Johnson & Johnson vaccine

Developer

The Janssen Pharmaceutical Companies of Johnson & Johnson developed the investigational vaccine (also known as Ad.26.COV2.S), a recombinant vector vaccine that uses a human adenovirus to express the SARS-CoV-2 spike protein in cells.

Description

This vaccine does not need to be stored at sub-zero temperatures, and it may require just a single dose. If its efficacy is similar to already authorised vaccines, it could become a champion in its category as much easier to handle.

Development phase

It is currently in phase III with 60,000 participants in USA, Argentina, Brazil, Chile, Colombia, Mexico, Peru and South Africa.

Regulatory status

The EMA started a rolling review on 1/12/2020. See here: https://www.ema.europa.eu/en/news/ema-starts-rolling-review-janssens-covid-19-vaccine-ad26cov2s

CansinoBio

Developer

CanSino Biologics Inc. and the Beijing Institute of Biotechnology

[2] Folegatti P. et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. The Lancet. 2020;396(10249):467-478. DOI: 10.1016/S0140-6736(20)31604-4.

Description

The AD5-nCoV vaccine candidate is a replication-defective adenovirus type 5 (viral vector) that expresses SARS-CoV-2 spike proteins (antigens). The platform (non-replicating viral vector) of AD5-nCoV was originally used for an Ebola vaccine (time to market minus 3 years).

Development phase

The first clinical phase 1 trial (ChiCTR2000030906/ NCT04313127) with 108 healthy adults is a single-centre dose-escalation study to test both the safety and tolerability of AD5-nCoV injections in three intervention groups using different dosages (low, medium and high). Specific T-cell response peaked at day 14 post-vaccination. (See results)[3]

As of 17 August, 2020 the results from the a phase 2 RCT were published:[4]

Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2.

Severe adverse reactions were reported by 24 (9%) participants in the 1×10^{11} viral particles dose group and one (1%) participant in the 5×10^{10} viral particles dose group. No serious adverse reactions were documented. Authors concluded that the Ad5-vectored COVID-19 vaccine at 5×10^{10} viral particles is safe, and induced significant immune responses in the majority of recipients after a single immunisation.

Inovio Ino-4800

Developer

Inovio Pharmaceuticals Inc.

[3] Zhu F et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. The Lancet. 2020;395(10240):1845-1854. DOI: 10.1016/S0140-6736(20)31208-3.

[4] Zhu F. et al. Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial. The Lancet. 2020;396(10249):479-488. DOI: 10.1016/S0140-6736(20)31605-6.

Description

Ino-4800 is a DNA plasmid vaccine based on a DNA platform. The DNA is hereby synthesised in a laboratory, hence, no actual virus samples are required.

The company's DNA platform was previously utilised for a MERS-CoV vaccine (INO-4700) tested in a phase I trial.

Development phase

A phase 1 clinical trial started in April 2020. The results are aimed to be presented and published later (April 2021).

The phase 1, non-randomised, open-label, sequential assignment clinical trial (NCT04336410) in 40 healthy adult volunteers aims to evaluate the safety, tolerability and immunological profile of INO-4800 administered by intradermal (ID) injection followed by electroporation (EP) using CELLECTRA® 2000 device.

Phase 1/2 trial (NCT04447781) aims to evaluate the safety, tolerability and immunological profile of INO-4800 administered by intradermal (ID) injection followed by electroporation (EP) using the CELLECTRA® 2000 device in 160 healthy adults aged 19 to 64 years in Republic of K

To date, no completed studies in humans are available for the INO-4800 vaccine candidate.

Novavax

Developer

Novavax and co-sponsored by Coalition for Epidemic Preparedness Innovations (CEPI)

Description

Recombinant protein nanoparticle technology platform that is to generate antigens derived from the coronavirus spike (S) protein. Novavax also expects to utilise its proprietary Matrix-M™ adjuvant in order to enhance immune responses.

Development phase

Novavax initiated a Phase 1/2 clinical trial in May/June 2020. Novavax has previous experience with both MERS and SARS.

The phase 1/2, randomised, placebo-controlled, triple-blind, parallel assignment clinical trial (NCT04368988) in 131 healthy adults aims to evaluate the immunogenicity and safety of SARS-CoV-2 rS nanoparticle vaccine with or without Matrix-M adjuvant in healthy participants ≥ 18 to 59 years of age.

An interim analysis of Part 1 safety and immunogenicity data will be performed prior to an optional expansion to Part 2.

To date, no completed studies in humans are available for Novavax COVID-19 vaccine.

GSK / Dynavax

Developer

Dynavax, Glaxo Smith Kline and the University of Queensland.

Description

The potential vaccine uses a molecular clamp stabilised Spike proteins. The so-called 'molecular clamp' technology is intended to prevent infection by synthesising surface proteins and „clamping" them into shape. In so doing, the immune system may induce a response, by recognising them as the correct antigen on the surface of the virus, more easily.

Initially, this technology was designed to be a platform for generating vaccines against different viruses such as influenza, Ebola, and the MERS coronavirus.

Development phase

A Phase 1 randomised, double blind, placebo-controlled, dosage-escalation trial started on July 13, 2020 (ACTRN12620000674932/NCT04495933). The estimated study completion date is September 2021.

To date, no completed studies in humans are available for the candidate vaccine.

CureVax

Description

A protamine-complexed mRNA-based vaccine expressing undisclosed SARS-CoV-2 protein(s). This means that CureVac's technology uses mRNA as a data carrier in order to train the human body to produce ideal levels of proteins. Thereby the immune system is stimulated and can respond to antigens

Development phase

Phase 1 (NCT04449276) study aims to evaluate the safety and reacto-genicity profile after 1 and 2 dose administrations of CVnCoV at different dose levels.

SinoVac

Developer

The private Chinese biopharmaceutical company Sinovac Biotech Ltd.

Description

CoronaVac, an inactivated COVID-19 vaccine candidate.

Development phase

The phase 1 and 2 trials started on April 16, 2020 in Jiangsu Province, China.

According to Sinovac announcement, preliminary phase I/II results showed that there was no serious adverse event after vaccinating a total of 743 volunteers. 90% seroconversion was observed in the phase II clinical trial 14 days after completion of a two-dose vaccination at day 0 and day 14

A Phase II study on elderly adults is being conducted which will be followed by child and adolescent groups. The phase II trial is expected to be completed at the end of 2020.

Sinovac registered a new Phase 3 RCT (NCT04456595), aiming at assessing efficacy and safety of the Adsorbed COVID-19 (inactivated) vaccine in health care professionals in Brazil. Estimated number of participants is 8,870.

Interim preliminary efficacy analysis can be triggered by reaching the target number of 150 cases. The study is estimated to be completed in October 2021.

China National Pharmaceutical Group Corporation (SINOPHARM)

Developer

Sinopharm is a state-owned Chinese company

Description

Vero-Cell is a β-propiolactone–inactivated whole-virus vaccine against COVID-19.

Development phase

A phase 3 double-blind, placebo controlled RCT has been initiated (ChiCTR2000034780), to evaluate the protective efficacy of inactivated SARS-CoV-2 Vaccine (Vero Cell) after full course of immunisation in healthy subjects aged 18 years old and above. The study is estimated to be completed in July 2021.

Sanofi-GSK

Developer

Sanofi developers a recombinant protein (technology already use for a flu vaccine) while GSK provides an adjuvant.

Development phase

A phase 1-2 randomised, double-blinded, placebo controlled trial is in progress with 440 participants (NCT04537208), recruiting in the USA only.

A phase 3 trial could be submitted end 2020.

Development is delayed as the immune response in the elderly population seems to be lower than expected, and more research needs to be done before launching the phase III confirmatory trial.

BCG Vaccine

Developer

Two research groups, one in the Netherlands, and one in Australia.

Description

Live attenuated virus: repurposing thee BCG vaccine, originally for tuberculosis, to fight SARS-CoV2 in healthcare workers at high risk.

Development phase

RCTs in Netherlands (BCG-CORONA phase 3 trial, NCT04328441) and Australia (BRACE phase 3 trial, NCT04327206) aim to assess whether BCG-Danish reduces the incidence and severity of COVID-19 in health-care workers, and the effect this has on days off work.

1,000 healthcare professionals to be enrolled in 8 hospitals to receive the vaccine or placebo.

Sputnik V Vaccine (Russia)

This Russian COVID-19 vaccine Sputnik V is the first in the world with a national authorisation for human use. It was approved for public use even ahead of its Phase III trial. No trial data are published.

Developer

Gamaleya Research Institute of Epidemiology and Microbiology,

Description

Gam-COVID-Vac is a viral two-vector vaccine based on the human adenovirus, a common cold virus, fused with the spike protein of SARS-CoV-2 to stimulate an immune response.

Development phase

Sputnik V is approved for distribution in Russia, despite having been tested only in a small number of people in early-stage clinical trials that lasted two months, normally a process requiring a year or more of clinical assessment for proof of vaccine safety and efficacy against viral disease.[5]

In fact, no phase 3 trial has started as of September 2020.

[5] "Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia". The Lancet: 1–11. 4 September 2020. doi:10.1016/S0140-6736(20)31866-3.

Initiatives of interest

Vaccine trials and initiatives

COVID-19 Prevention Trial Network (COVPN)

NIAID established a new clinical trials network - The COVID-19 Prevention Trials Network (COVPN), that aims to enroll thousands of volunteers in large-scale clinical trials testing a variety of investigational vaccines and monoclonal antibodies intended to protect people from COVID-19.

The first Phase 3 clinical trial that the COVPN is expected to conduct with the investigational mRNA-1273 vaccine, developed by NIAID scientists and their collaborators at Moderna, Inc., based in Cambridge, Massachusetts.[6]

ACCESS (vACcine Covid-19 monitoring ReadinESS)

Utrecht scientists (in close collaboration with RIVM, Netherlands Pharmacovigilance centre LAREB and the PHARMO Institute in the Netherlands) are leading an European project with the aim to create an infrastructure and to prepare European organisations to collaboratively evaluate the benefits, coverage and risks of the novel COVID-19 vaccines in their post-licensure phase. The project is funded by the European Medicines Agency (EMA).[7]

COVAX

The COVAX initiative consists in purchasing distributing fairly two billion vaccine doses in 2021. It emerged from the World Health Organization (WHO), the Coalition for Epidemic Preparedness Innovations (CEPI) and from GAVI, the Vaccine Alliance.

NIAID Vaccine Research Centre

Almost of developments of SARS-coV2 vaccines derive from research for an HIV vaccine.[8]

[6] https://www.nih.gov/news-events/news-releases/nih-launches-clinical-trials-network-test-covid-19-vaccines-other-prevention-tools
[7] https://www.uu.nl/en/news/monitoring-the-benefits-and-safety-of-the-new-corona-vaccines
[8] Barney Graham, Deputy Director, Vaccine Research Centre